REMARKS

With this amendment, claims 14, 17, 20, 22, 39, 42, 45-47, and 58 have been amended for clarity. In addition, typographical errors in the specification have been corrected. No new matter has been added by virtue of these claim amendments or the amendments to the specification. Upon entry of the present amendments, claims 14, 15, 17, 20-22, 39, 40, 42, 45-47, and 58 will be pending in the above-identified application.

The 35. U.S.C. § 112 SECOND PARAGRAPH REJECTION SHOULD BE WITHDRAWN

The Examiner has rejected claims 14, 15, 17, 20-22, 39, 40, 42, 45-47, and 58 under 35 U.S.C. § 112, second paragraph, for lack of antecedent basis for the phrase "said genotypic data structure" in independent claims 14, 17, 20, 22, 39, 42, 45-47, and 58. In response, Applicants have amended these independent claims to provide antecedent basis for this term. For example, in claim 14, Applicants have amended the claim to indicate that the repeating step establishes a plurality of genotypic data structures. Then, the identifying step identifies one or more genotypic data structures from this plurality of genotypic data structures. In light of these claim amendments, Applicants believe that all instances of the phrase "said genotypic data structure" or "the genotypic data structure" have proper antecedent basis.

The Examiner has rejected claim 46 under 35 U.S.C. § 112, second paragraph, for lack of antecedent basis for the phrase "said function." Applicants have amended claim 46 to remove the clause that begins with the phrase "said function." Therefore, this 35 U.S.C. § 112, second paragraph, rejection of claim 46 is now moot.

The Examiner has rejected claim 46 under 35 U.S.C. § 112, second paragraph, for use of the abbreviation "Z". Applicants have amended claim 46 to remove any reference to the abbreviation "Z". Therefore, this 35 U.S.C. § 112, second paragraph, rejection of claim 46 is now moot.

In view of the above-identified claim amendments, Applicants believe that each of the 35 U.S.C. § 112, second paragraph, rejections raised by the Examiner have now been obviated. Accordingly, Applicants respectfully request that the 35 U.S.C. § 112, second paragraph, rejection of the pending claims be withdrawn.

The 35. U.S.C. § 101 REJECTION SHOULD BE WITHDRAWN

The Examiner has rejected claims 14, 15, 17, 20-22, 39, 40, 42, 45-47, and 58 under 35 U.S.C. § 101 because the claimed invention is allegedly directed to non-statutory algorithm type subject matter. For the reasons discussed below, Applicants respectfully traverse the rejection.

Before addressing the 35 U.S.C. § 101 rejection, Applicants would like to discuss the characterization of the invention provided by the Examiner when making the 35 U.S.C. § 101 rejection. Specifically, in point 13 of the October 19, 2004 Office Action, the Examiner stated that the instant invention is directed to a computer program product and a product comprising processes for manipulating genotypic and phenotypic data. Applicants disagree with this characterization of the invention. First, many of the claims in the pending application are method claims. Such method claims can be performed in any manner, using a computer or otherwise. As such, many aspects of the present invention are not computer programs or products. Second, the Examiner's characterization of the invention as one that manipulates genotypic and phenotypic data is somewhat abstract. Rather, the invention is better characterized as one that is directed to the practical application of associating a phenotype with one or more chromosomal regions in the genome of a species.

In making the 35 U.S.C. § 101 rejection, the Examiner assumes that, in order to be patentable subject matter, a computer-related process claim requires a physical alteration step. Applicants do not understand why the Examiner is applying this supposed computer-related process claim to claims 14, 15, 17, and 20-22, which are method claims. Furthermore, as set forth in section 2106(IV)(B)(2)(b) of the M.P.E.P., the test for patentability of computer-related processes provides an additional avenue for patentablity:

> To be statutory, a claimed computer-related process must either: (A) result in physical transformation outside the computer for which a practical application in the technical arts is either disclosed in the specification or would have been known to a skilled artisan (discussed in i) below), or (B) be limited to a practical application within the technological arts (discussed in ii) below).

Thus, contrary to the Examiner's assertions, even if a claimed computer-related process does not recite a physical alteration step that occurs outside of the computer, the process is still patentable if it is limited to a practical application within the technical arts. The instant claims are directed to methods, computer program products, and computer systems that are

designed for the practical application of associating a phenotype with one or more candidate chromosomal regions. By practicing the instant claims, a phenotype is associated with one or more candidate chromosomal regions. The invention has significant practical application in a number of different areas including elucidation of the genetic basis of a variety of complex diseases. As such, the claims recite a concrete, tangible and useful result, pursuant to section 2106(IV)(B)(2)(b)(ii) of the M.P.E.P. Accordingly, Applicants respectfully request that the 35 U.S.C. § 101 rejection of claims 14, 15, 17, 20-22, 39, 40, 42, 45-47, and 58 be withdrawn.

The 35. U.S.C. § 103 REJECTION SHOULD BE WITHDRAWN

The Examiner has rejected claims 14, 15, 39, 40 and 46 under 35 U.S.C. § 103 as being unpatentable over Satagopan *et al.*, Genetics 144, pages 805-816, 1996 ("Satagopan") in view of Almasy *et al.*, Am J. Hum. Genet. 62, pages 1198-1211, 1998 ("Almasy"). As will be explained below, Applicants respectfully believe that the Examiner has mischaracterized Satagopan and Almasy. In so doing, the Examiner equates the mischaracterized teachings of Satagopan and Almasy with certain elements of Applicants' claims in order to incorrectly arrive at the 35 U.S.C. § 103 rejection.

Specifically, in point 18 of the October 19, 2004 Office Action, the Examiner states that page 809, column 2, lines 29-47, of Satagopan teaches the comparison of two models to a correlation value where the ratio of marginal probabilities of the two compared models is a Bayes factor. The Examiner states that this is equivalent to the comparison step of claims 14, 39, and 46 (rewritten as a determining step in these claims as amended in the instant response). Applicants respectfully point out that the cited passage in Satagopan does not teach or suggest the comparison of a phenotypic model to a genotypic model as recited in Applicants' claims 14, 39, and 46. What is being compared in Satagopan is a first QTL model to a second QTL model. A Bayes factor is computed in this comparison. As explained on page 810, column 2, first full paragraph, and detailed in Table 1 of Satagopan, the value of the Bayes factor computed using equation 15 indicates whether the first QTL model or the second QTL model fits the data better. As described on Satagopan page 811, columns 1 and 2, bridging paragraph, equation 15 was used to determine whether genetic data from *Brassica napus* should be fit with a no-QTL model, a one-QTL model, a two-QTL model, or a three-QTL model. For example, a two-QTL model means that the *Brassica napus* phenotypic data is best explained by two loci (QTL) in the *Brassica napus* genome

whereas a three-QTL model means that the *Brassica napus* phenotypic data is best explained by three loci (QTL) in the *Brassica napus* genome. By performing the model comparisons in accordance with equation 15, Satagopan determined that the two-QTL model best explains the data. See, for example, Satagopan, page 814, column 2, first full paragraph ("[a]ll three approaches to estimate Bayes factors favored a two QTL model over a single QTL model").

Moreover, contrary to the Examiner's assertions in point 18 of the October 19, 2004 Office Action, page 809, column 2, lines 29-47, of Satagopan does not teach the computation of a correlation value as recited in Applicants' claims 14, 39, and 46. Rather, what is being computed by Satagopan in the cited passage is a Bayes factor. A Bayes factor is not a correlation value.

In point 19 of the October 19, 2004 Office Action, the Examiner equates page 814, column 2, lines 4-10, of Satagopan to the repeating step recited in Applicants' claims 14, 39, and 46. Applicants respectfully submit that the repetition that occurs in the cited passage of Satagopan has nothing to do with the repetition recited in Applicants' claims 14, 39, and 46. In Applicants' claims, an establishing and determining step is repeated for each loci in a plurality of loci. In contrast, in Satagopan's repeating step, a Markov chain is repeated in order to test the stability of an estimate of a Bayes factor that is used by Satagopan to determine whether one genotypic model is better than another genotypic model. As such, Applicants' repeating step cannot be equated to Satagopan's equating step. In Applicants' repeating step, a different loci in a plurality of loci is being tested. In Satagopan, the same data is being retested in order to obtain confidence in an estimate of a Bayes factor. In Applicants' repeating step, a genotypic structure corresponding to a different loci in a plurality of loci is compared to a phenotypic data structure in order to determine a correlation value for the genotypic data structure. No such correlation value is determined in Satagopan's repeating step.

In point 20 of the October 19, 2004 Office Action, the Examiner asserts that the term "center of the locus" as recited in claims 14 and 39 is not specifically defined in the specification. Applicants respectfully note that a locus is a region of a genome. See, for example, page 15, lines 19-32, of Applicants' specification. As such, it is well known in the art that the center of a locus is the center of the region of the genome defined by the locus. Accordingly, no definition for "the center of the locus" need be provided in the specification for one of skill in the art to understand the metes and bounds of the claimed invention. Moreover, this definition is consistent with the examples provided in the specification, which

describe how the distance from the center of a loci, as measured in centiMorgans, is used in a weighting function. See, for example, page 18, line 13, through page 20, line 16, of Applicants' specification. Moreover, page 20, lines 2-12, of Applicants' specification provide a specific method for determining distance from the center of a loci. There, Applicants define distance from the center of a loci in terms of probability in a Gaussian distribution centered on the center of the loci. Thus, the phrase "the center of the locus" is well defined both in the art and in Applicants' specification.

The Examiner somehow equates the center of a locus, and a weighting scheme based on distance away from the center of a locus, as recited in Applicants' claims 14 and 39, to a method for parameter estimation found on page 802, column 2, of Satagopan. But the parameter estimation of Satagopan simply cannot be equated to the weighting scheme recited in Applicants' claims 14 and 39 because such parameter estimation has nothing to do with the claimed invention. The cited section of Satagopan, parameter estimation, is merely describing a method to circumvent a requirement to find exact solutions to high-dimensional integrals in a Bayesian approach to fitting a multi-locus model to quantitative trait and molecular marker data. Applicants' claims 14 and 39 have nothing to do with such a Bayesian approach. In essence, the Examiner is comparing apples to oranges to arrive at the instant rejection.

Such improper comparison of Satagopan and the instant claims continues in point 21 of the October 19, 2004 Office Action. There the Examiner states that the Gaussian distributions described on page 811, column 2, lines 7-9, of Satagopan can somehow be equated to the Gaussian distribution recited in Applicants' claims 15 and 40. This is not the case. Applicants' Gaussian distribution defines a probability function about the center of a locus as described, for example, on page 20, lines 2-10, of Applicants' specification. As indicated in the cited section of Applicants' specification, the lower the probability a given locus position **x** is from the center of a given locus L, as determined by the Gaussian distribution about the center of locus L, the smaller the weight that will be assigned to the given locus position **x**. In complete contrast, page 811, column 2, lines 7-9, of Satagopan merely states that the residual error in a model for the number of days to flowering for the i^{th} DH line falls into a Gaussian distribution. The Gaussian distribution in the residual error in a model for the number for days to flowering cannot possibly have anything to do with Applicants' claimed weighting scheme that employs a Gaussian distribution in order to quantify distance from the center of a locus.

In point 22 of the October 19, 2004 Office Action, the Examiner rejects the limitations of claim 46, lines 27-29, in view of previously identified citations from Satagopan. In response, Applicants would like to point out that this limitation in claim 46 has been deleted in the present amendment, rendering this rejection of claim 46 moot.

In point 23 of the October 19, 2004 Office Action, the Examiner notes that Satagopan does not describe the limitation of weighting each variation wherein variations further from the center are "downweighted." Such a limitation appears in pending claims 14 and 39. To remedy the deficiency in Satagopan, the Examiner relies on Almasy. In point 24, the Examiner alleges that page 1201, column 2, lines 7-10, of Almasy teaches that "the results from well known in the art methods can be averaged by the use of the likelihood of the imputed marker genotype vector as a weighting factor." Applicants respectfully note that this passage in Almasy is simply referring to a method for populating an Identity by Descent (IBD) matrix $\hat{\Pi}_i$, which is defined on column 1, page 1200 of Almasy, as the matrix whose elements (π_{ijl}) provide the predicted proportions of genes that individuals j and l share IBD at a QTL that is linked to a genetic maker locus. Such a matrix, and any weighting schemes used in the preparation of such a matrix, have nothing to do with Applicants' recited weighting limitations. As such, Almasy does not teach or suggest any of the weighting limitations in the pending claims. Similarly, the discussion of a k_2-Correlation function for incorporating dominance on page 1205, column 1, lines 3, to column 2, line 3, and Figure 3 of Almasy has nothing to do with Applicants claimed weighting schemes.

As an additional matter, Satagopan and Almasy do not teach specific limitations found in claims 14, 39 and 46. For example, claims 14, 39, and 46 recite using a phenotypic data structure that comprises a *difference* in a phenotype between different strains of the species. Such a difference is explained, *inter alia*, on page 14, lines 1-17 of the specification, which, for the Examiner's convenience is reproduced below:

> As an example, consider phenotypic information on the lifespan of five mouse strains:

Strains	Lifespan (days)
A/J	777
AKR/J	282
C3H/HeJ	510
C57BL/6J	895

DBA/2J	568

An exemplary phenotypic distance matrix that tracks the lifespan for these five species members has the form:

P	A/J	AKR/J	C3H/HeJ	C57BL/6J	DBA/2J
A/J	0	495	267	118	209
AKR/J	495	0	228	613	286
C3H/HeJ	267	228	0	385	58
C57BL/6J	118	613	385	0	327
DBA/2J	209	286	58	327	0

Each value in this illustrative phenotypic distance matrix represents the difference in life span between the designated members.

The phenotypic data structure derivation subroutine 46 converts the phenotypic matrix to the phenotypic array by taking the non-redundant, non-diagonal elements of the matrix and arranging them into a vector *P*:

$$P \equiv p(1,2), p(1,3), \ldots, p(1,N), p(2,3), p(2,4), \ldots, p(2,N), \ldots p(N-1, N)$$

The vector *P* obtained for the illustrative distance matrix set forth above is *P* = (495, 267, 118, 209, 228, 613, 286, 385, 58, 327). The linear format of *P* facilitates the ordered comparison of the phenotype and genotype of respective strains of an organism of interest in subsequent computational steps.

To summarize, Satagopan and Almasy, either alone or in combination, do not teach or suggest a phenotypic data structure that comprises a *difference* in phenotype between different strains of a species.

Based on the above discussions, Satagopan and Almasy, either alone or in combination, do not recite each and every limitation of the rejected claims. Accordingly, Applicants request that the 35 U.S.C. § 103 rejection of claims 14, 15, 39, 40, and 46 be withdrawn.

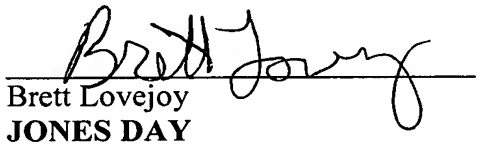
CONCLUSION

In view of the above remarks, Applicants respectfully submit that the subject application is in good and proper order for allowance. Withdrawal of the Examiner's rejections and objections and early notification to this effect are earnestly solicited.

No fee is believed owed in connection with filing of this amendment and response. However, should the Commissioner determine otherwise, the Commissioner is authorized to charge any underpayment or credit any overpayment to Jones Day Deposit Account No. 50-3013 for the appropriate amount. A copy of this sheet is attached.

Respectfully submitted,

Date: May 3, 2005



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